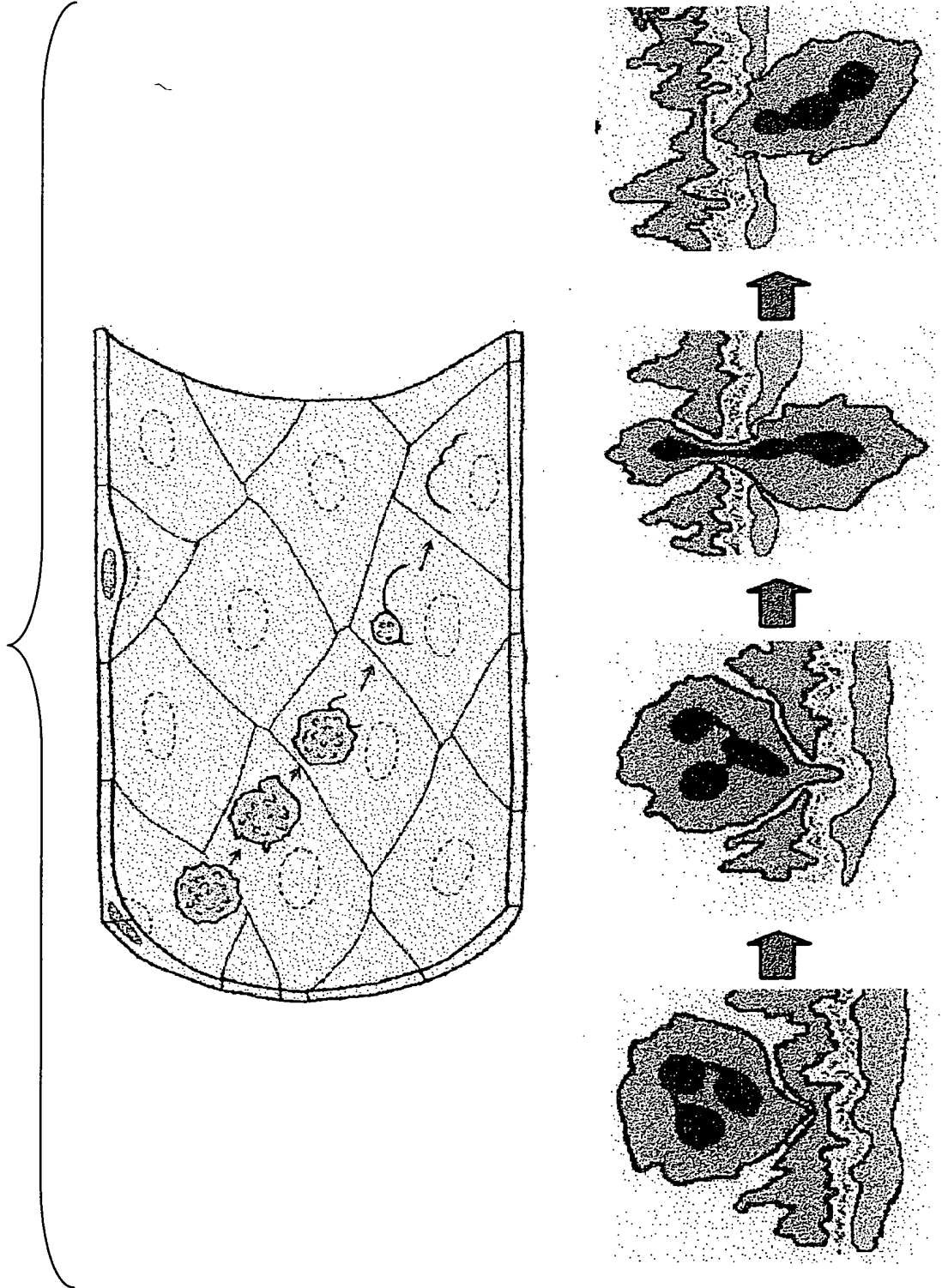
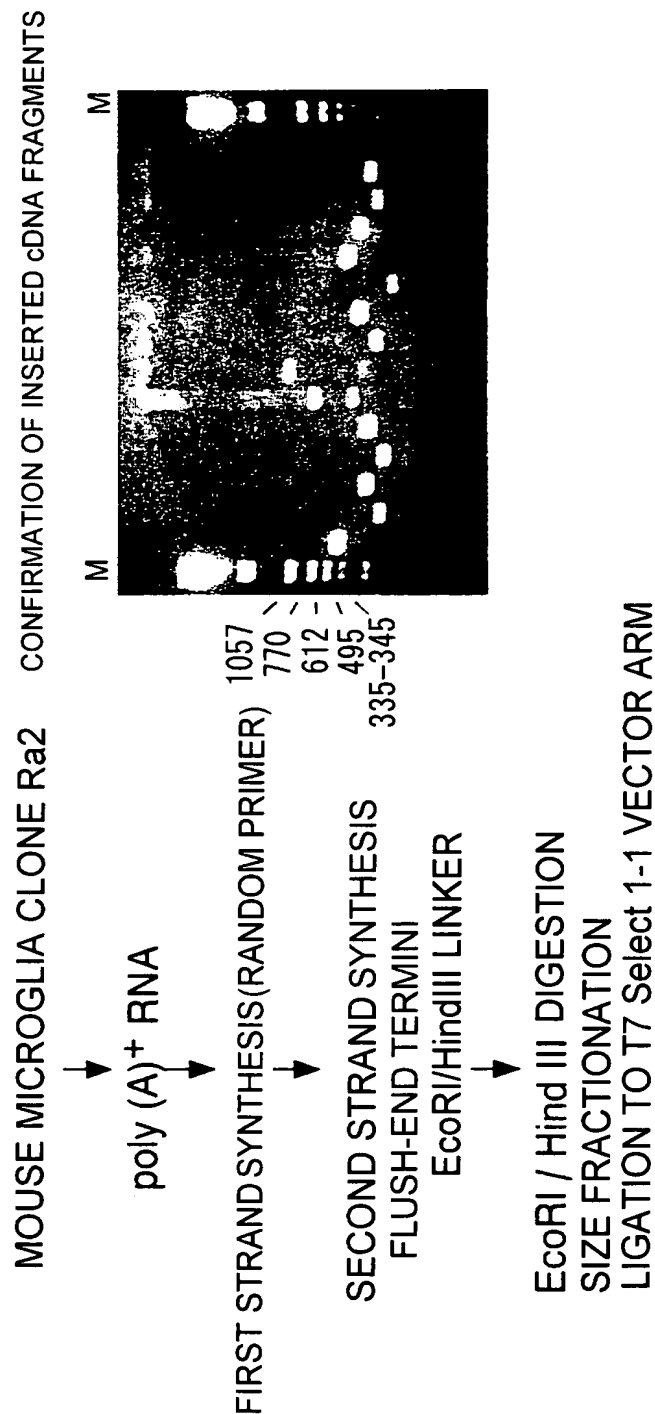
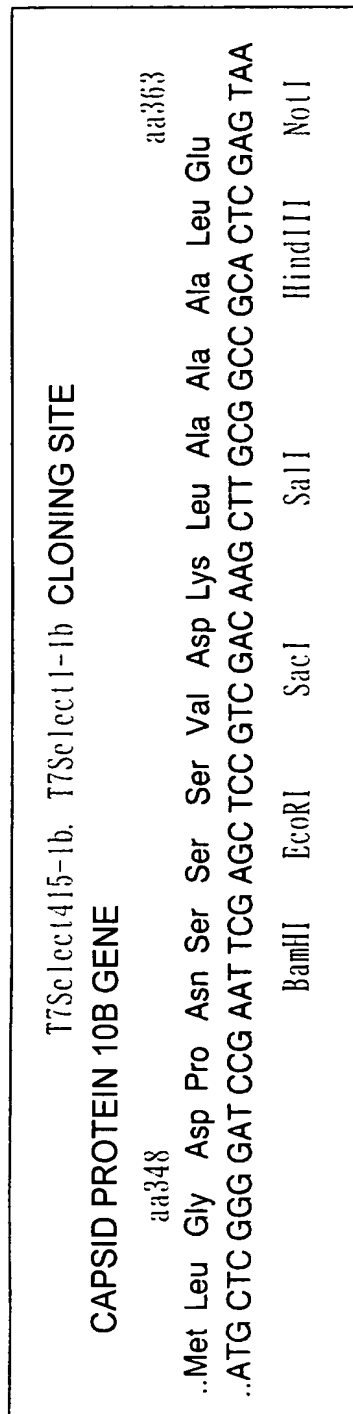


FIG. 1



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# FIG. 2



T7Select4I5-1b, T7Select1-1b CLONING SITE

aa348

....Met Leu Gly Asp Pro Asn Ser Ser Ser Val Asp Lys Leu Ala Ala Ala Leu Glu  
 ....ATG CTC GGG GAT CCG AAT TCG AGC TCC GTC GAC AAG CTT GCG GCC GCA CTC GAA

• SYNTHETIC

OLIGONUCLEOTIDE-1 (84mer)

**45 BASES (15 a.a.)**

Asn Cys X X X X Cys Lys Leu  
 GCCCAGCGGCCAATTGCNNKNNK—NNKNNKTGCAAGCTTGCGGCCGCAAGT  
 Mun I Hind III

**.SYNTHETIC**

OLIGONUCLEOTIDE -2 (81mer)

**45 BASES (15 a.a.)**

Asn Ser X X X Lys Leu  
CAGCCGGCCTCGAATTCNNKNK——NNKNKAGCTTGCGCGCAGGT  
EcoR I | Hind III

ECORI

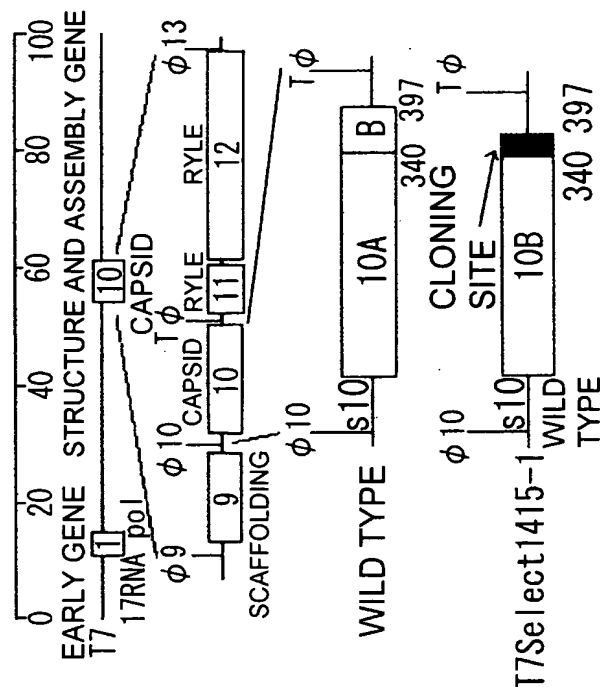
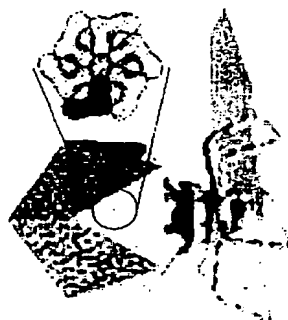
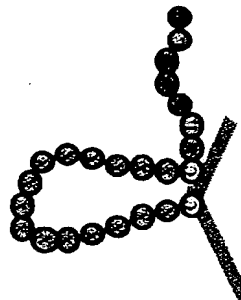
### Hind III

N: G, A, T, C MIXTURE  
K: G, T MIXTURE

PCR AMPLIFICATION  
RESTRICTION ENZYME DIGESTION  
LIGATION TO T7Select 415-1 VECTOR ARM

# T7 Select SYSTEM

- T7Select415-1
  - IN WILD TYPE, PARTS OF THE CAPSID ARE PRODUCED FROM 10A AND 10B BY FRAMESHIFT. HEREIN, THE CAPSID IS MADE OF ONLY 10B.
  - 415 PEPTIDES CAN BE DISPLAYED ON THE EXTERIOR OF THE CAPSID AS LONG AS THEY ARE UNDER 50 aa.
- 415-c15c LIBRARY
  - Cys-FLANKED 15-aa RANDOM PEPTIDES WERE INSERTED.
    - TGCNNKNNKNNKNNKNNKNNKNNKNNK
    - NNKNNKNNKNNKNNKNNKNNKNNKTGC
    - K=GorT, N=A, C, G or T
  - VARIANT=ABOUT 10<sup>7</sup>



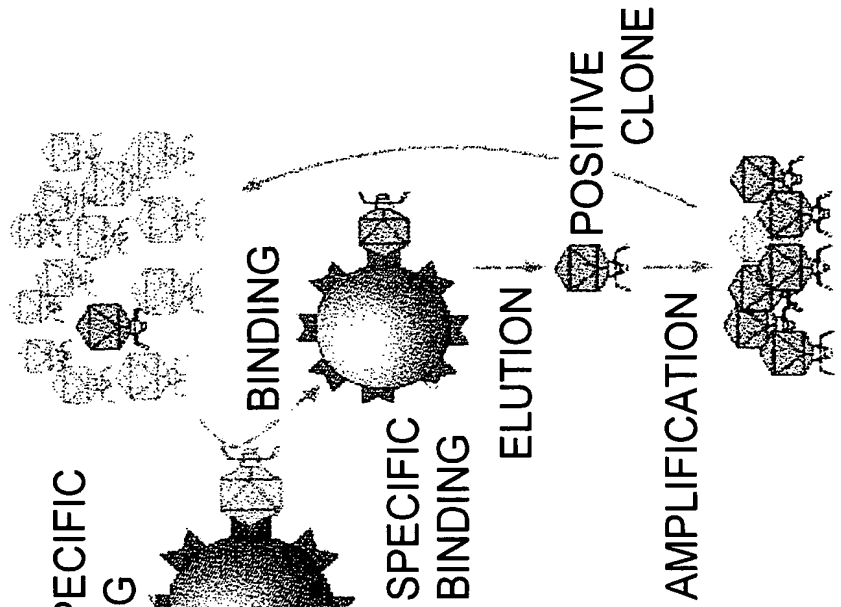
# FIG. 5

## PANNING METHOD

### • SELECTION METHOD UTILIZING PROTEIN INTERACTION

- SELECTIVE CONCENTRATION OF CELL SURFACE-ADSORBED PHAGES
- IMPORTANT PARAMETERS
  - CARRIER SELECTION
  - ADSORPTION CONDITIONS
  - REMOVAL OF NON-SPECIFICALLY-BOUND PHAGES
  - PHAGE VS CELL
  - PHAGE VS PROTEIN OR LYSATE

### T7 select LIBRARY



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# FIG. 6

## SCHEDULE

020425 : INJECTION OF CONTROL PHAGE (No.145) INTO TAIL VEIN

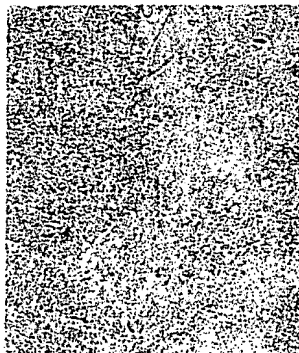
INJECTION OF Exp PHAGE INTO TAIL VEIN: (No.89 (SAME ARRANGEMENT AS IN #2))



5 MINUTES AFTER EUTHANASIA, 60 MINUTES AFTER EUTHANASIA  
(BRAIN, LUNG, LIVER, SPLEEN, KIDNEY, TESTIS)

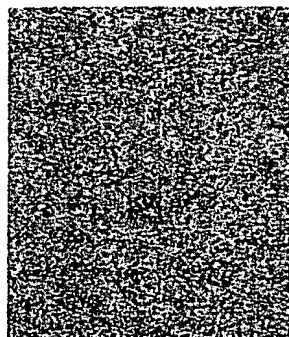
### 28rRNA PHASE

#### PHASE



BRAIN STEM

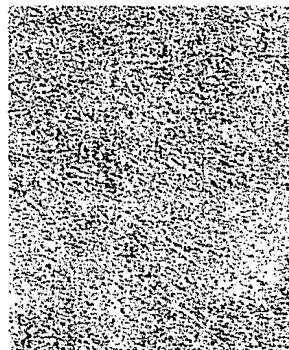
#### PHASE



CALLOSUM

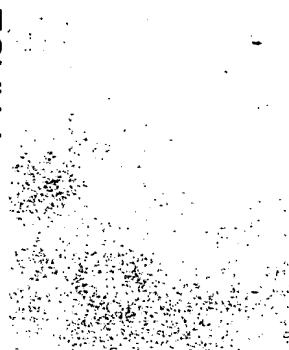
### #2 PHASE

#### PHASE

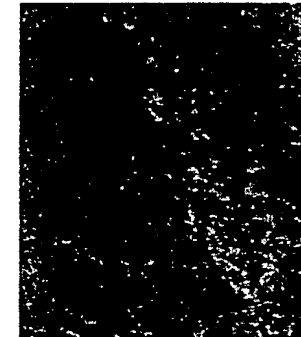
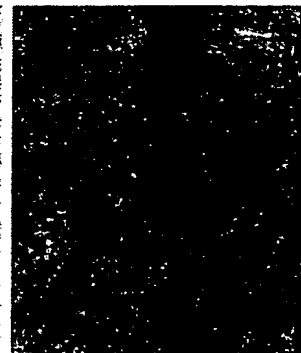


BRAIN STEM

#### PHASE



CALLOSUM



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Title: POLYPEPTIDES HAVING BRAIN-LOCALIZING  
ACTIVITY AND USES THEREOF (As Amended)

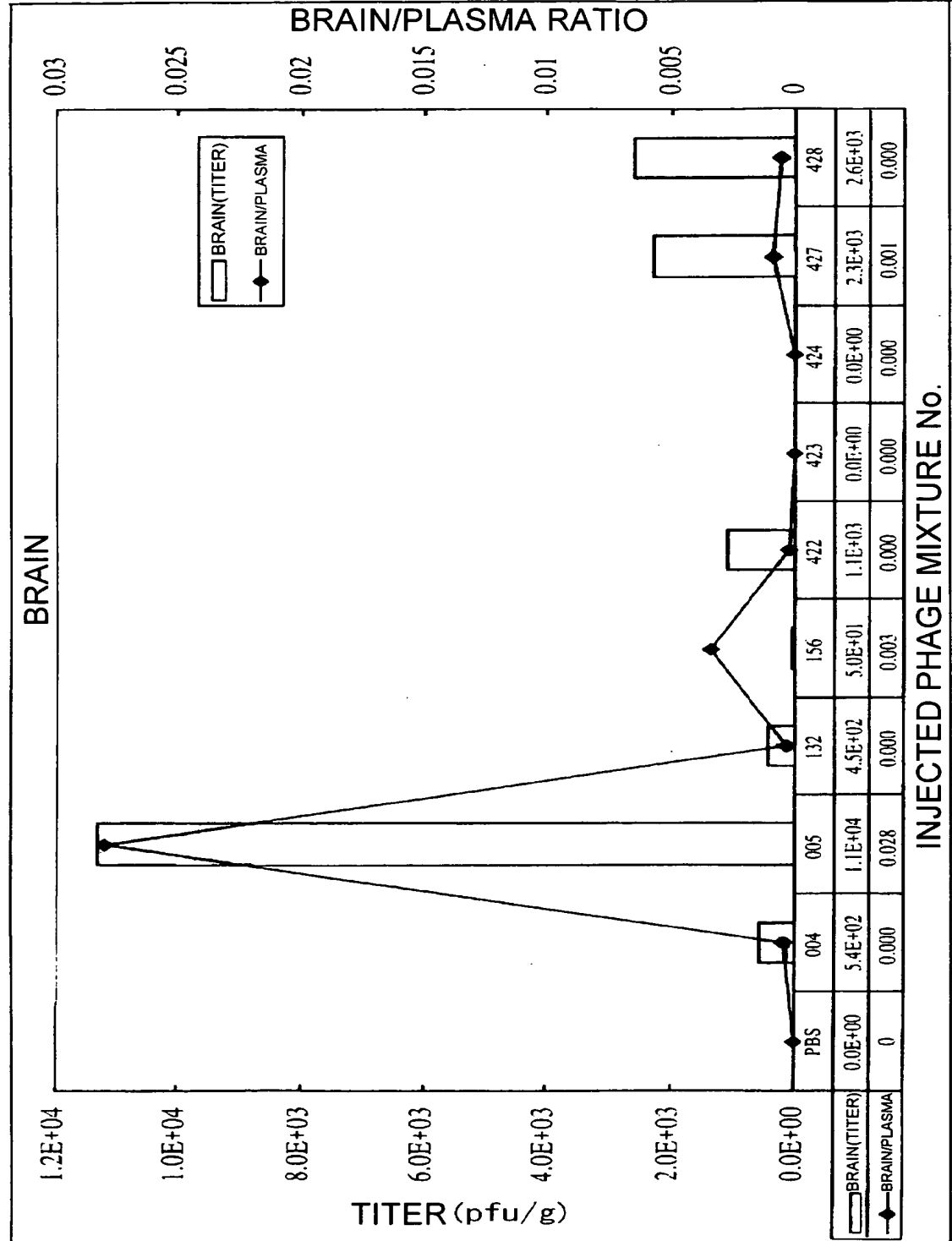
Inventor(s): Makoto SAWADA

DOCKET NO.: 084335-0201

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ACTIVITY AND USES THEREOF (As Amended)  
Inventor(s): Makoto SAWADA  
DOCKET NO.: 084335-0201

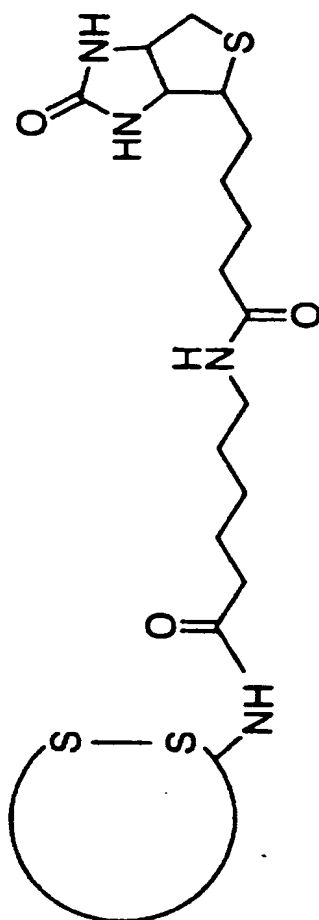
FIG. 7



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Title: POLYPEPTIDES HAVING BRAIN-LOCALIZING  
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Inventor(s): Makoto SAWADA  
DOCKET NO.: 084335-0201

FIG. 8



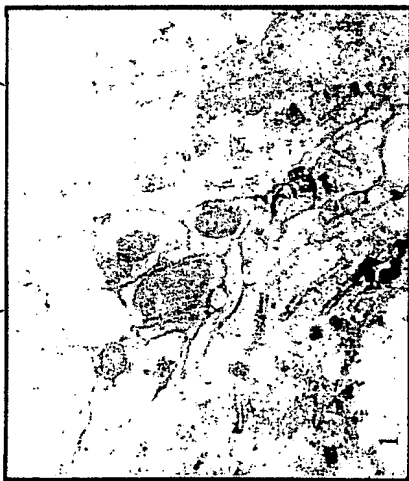
BIOTIN



FIG. 9

CONTROL

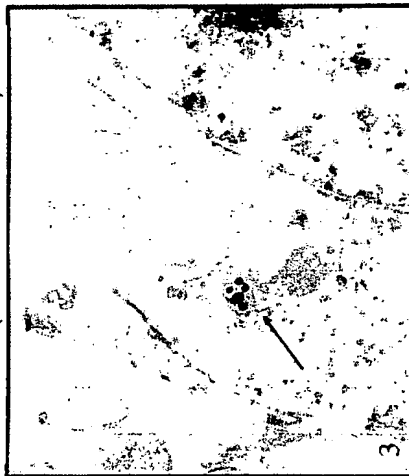
HIPPOCAMPAL PYRAMIDAL  
CELLS (CA1-CA2 REGION)



1

BIOTIN -T2J002

HIPPOCAMPAL PYRAMIDAL  
CELLS (CA1-CA2 REGION)



3

BIOTIN -T2J004

HIPPOCAMPAL PYRAMIDAL  
CELLS (CA1-CA2 REGION)



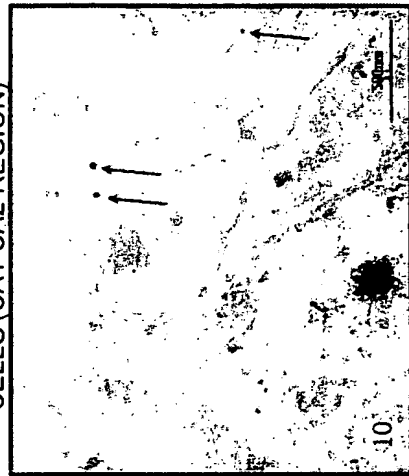
9

HIPPOCAMPAL PYRAMIDAL  
CELLS (CA1-CA2 REGION)



5

HIPPOCAMPAL PYRAMIDAL  
CELLS (CA1-CA2 REGION)



10

CEREBELLAR PURKINJE  
CELL REGION



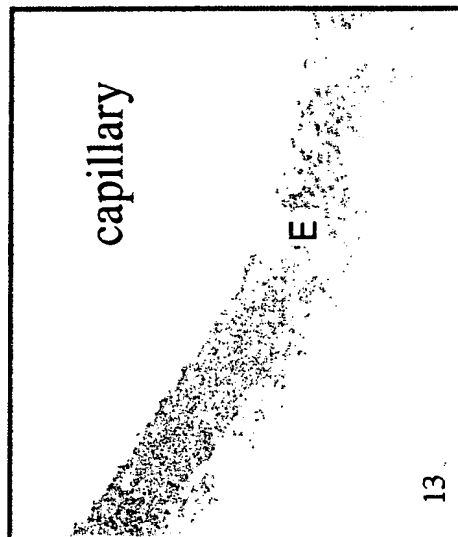
2

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FIG. 10

CONTROL  
(AVIDIN-COLLOIDAL GOLD)  
BIOTIN -T2J002  
COLLOIDAL GOLD  
CONJUGATE  
BIOTIN -T2J002



13



6

500nm



14

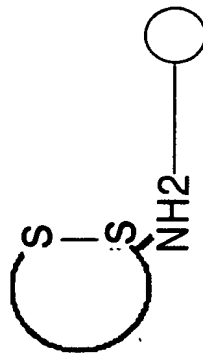
100nm

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FIG. 11

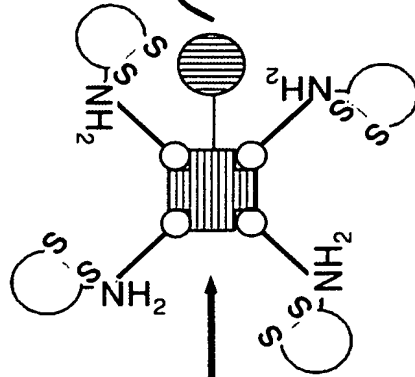
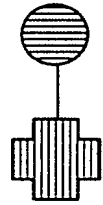
# METHOD

BIOTINYLATED CYCLIC  
PEPTIDE 004



+

AVIDIN -FITC



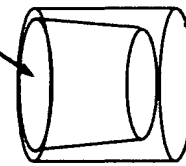
MBEC4

$1.26 \times 10^4$  CELLS /  $250 \mu\text{l}$

END-D

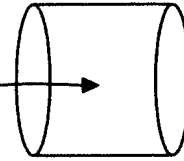
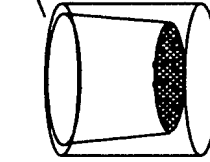
$2 \times 10^4$  CELLS /  $250 \mu\text{l}$

4 DAYS IN  
CULTURE MEDIUM

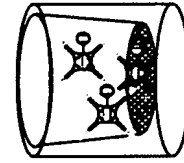


24 WELL  
PLATE  
(BD, 353504)

TRANSFERRED TO  
A NEW WELL



$750 \mu\text{l}$  DMEM 10% SERUM  
OR END-D MED.



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FIG. 12

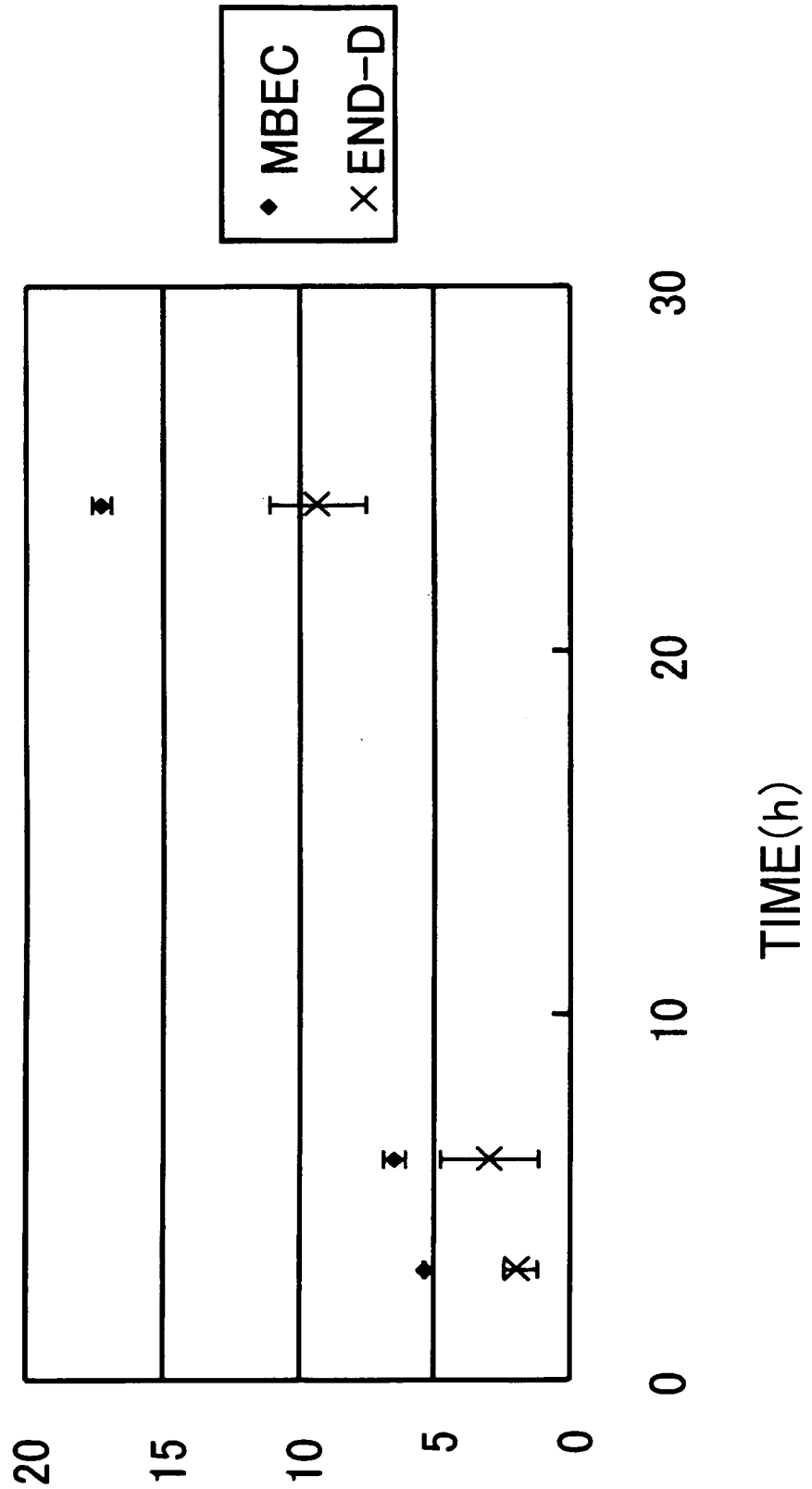
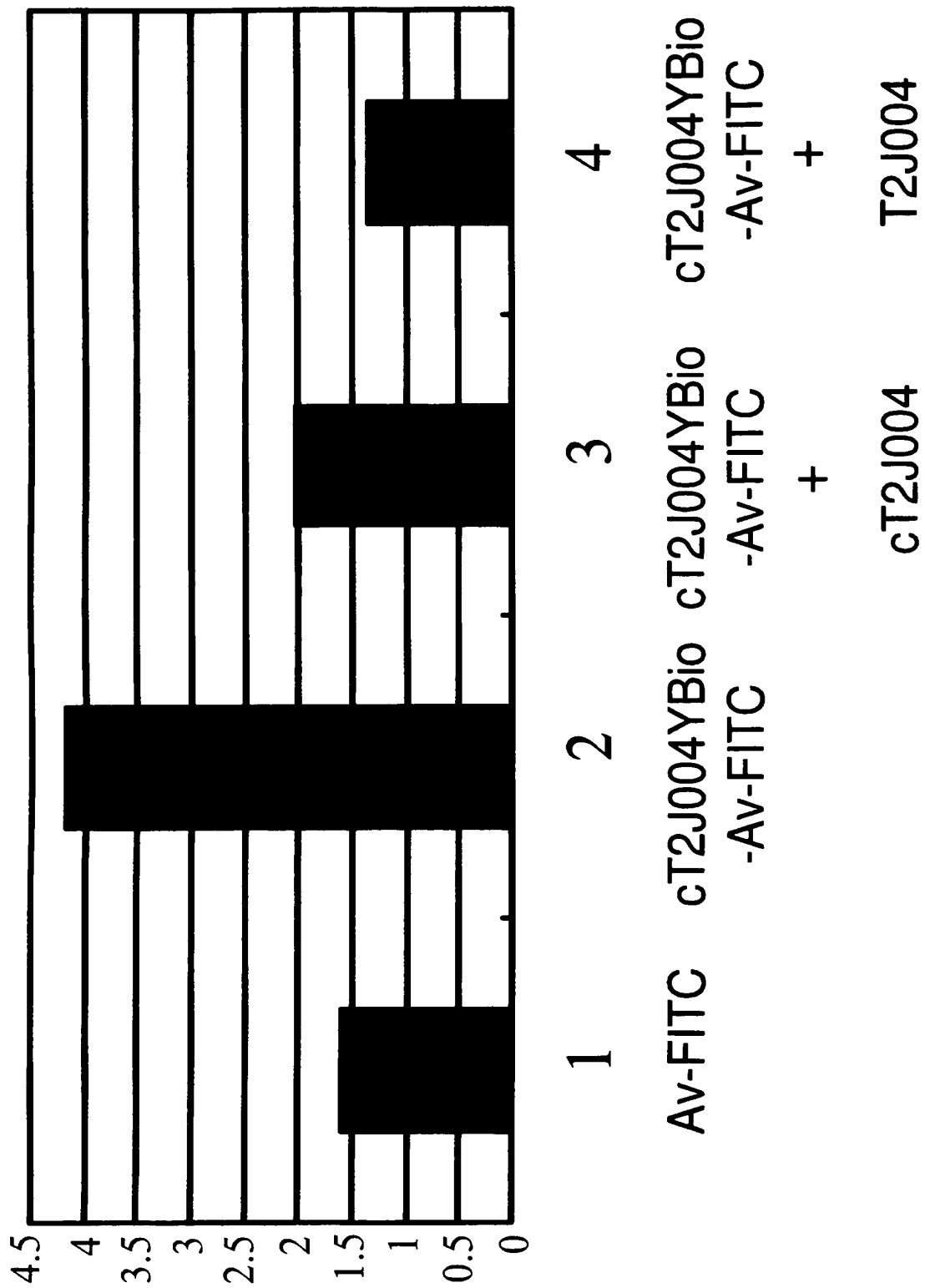
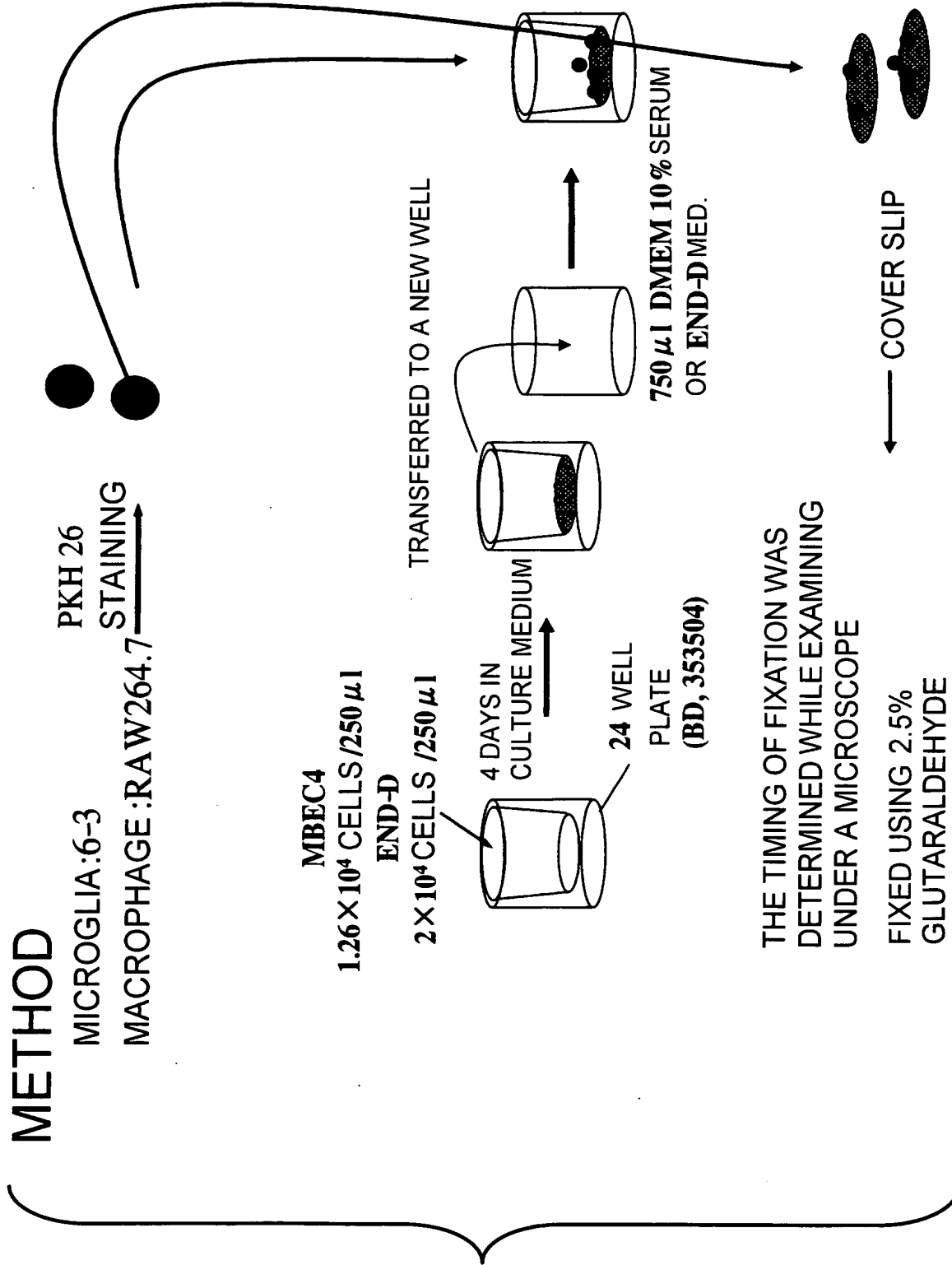


FIG. 13



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FIG. 14



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FIG. 15

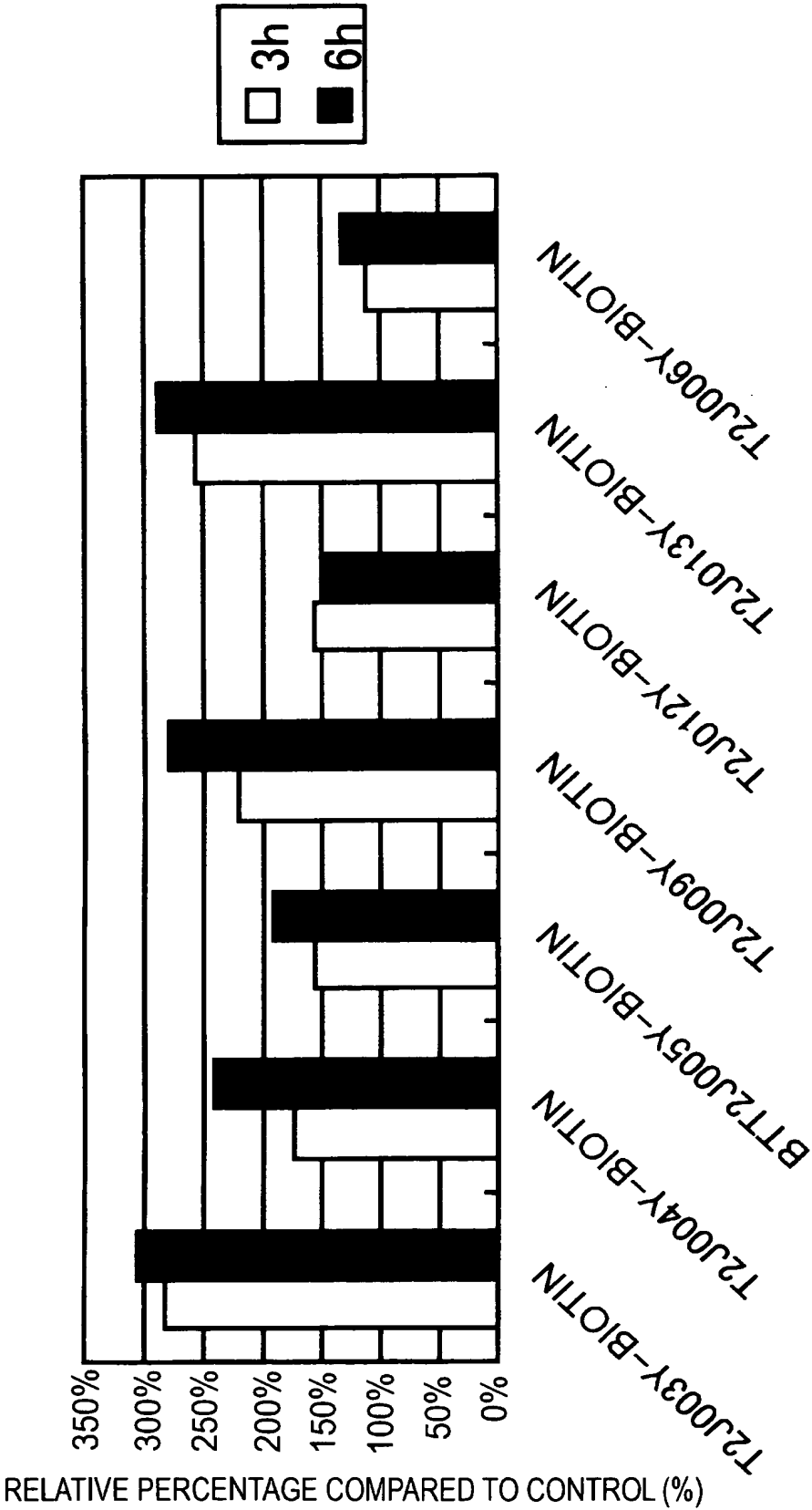


FIG. 16

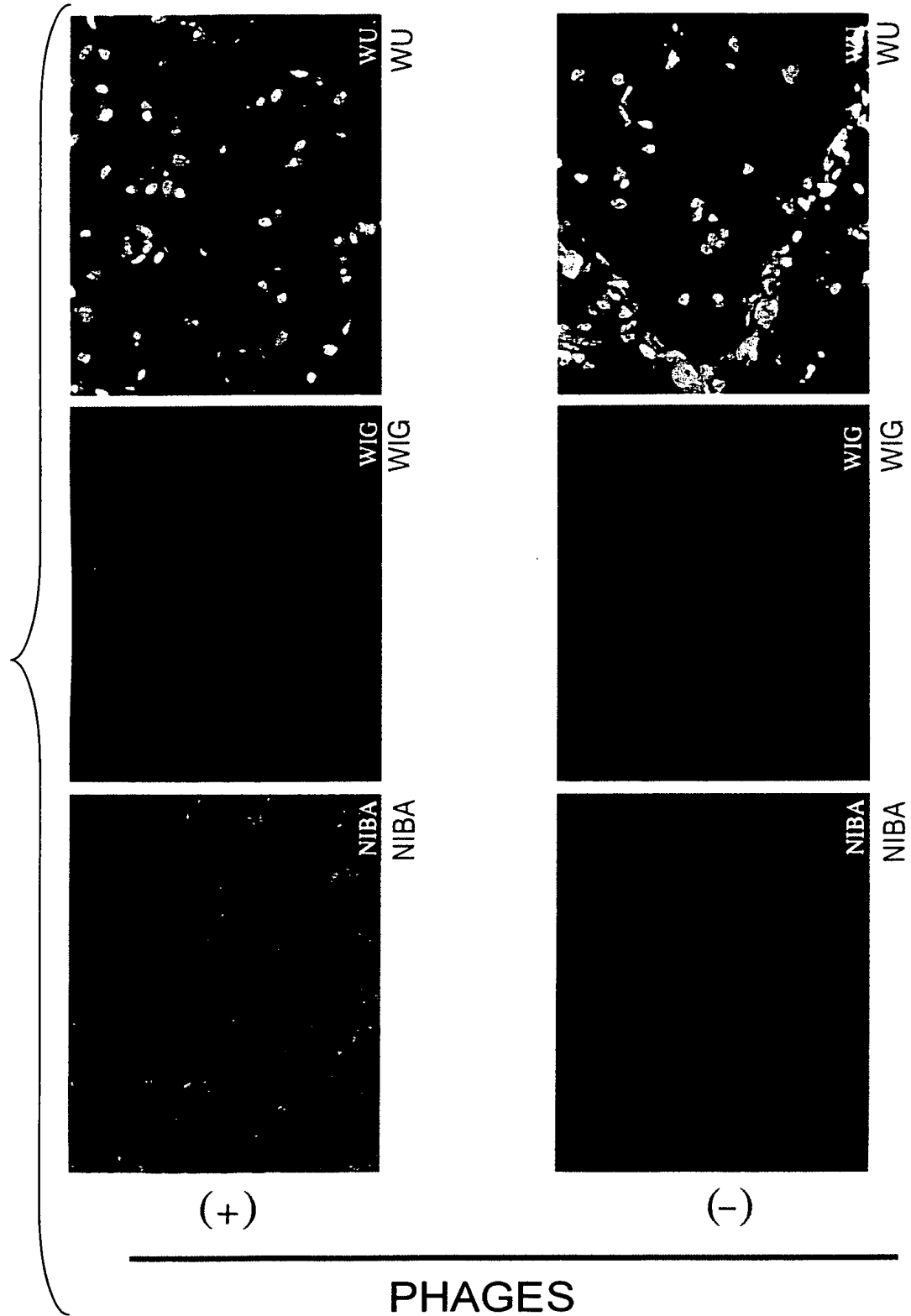
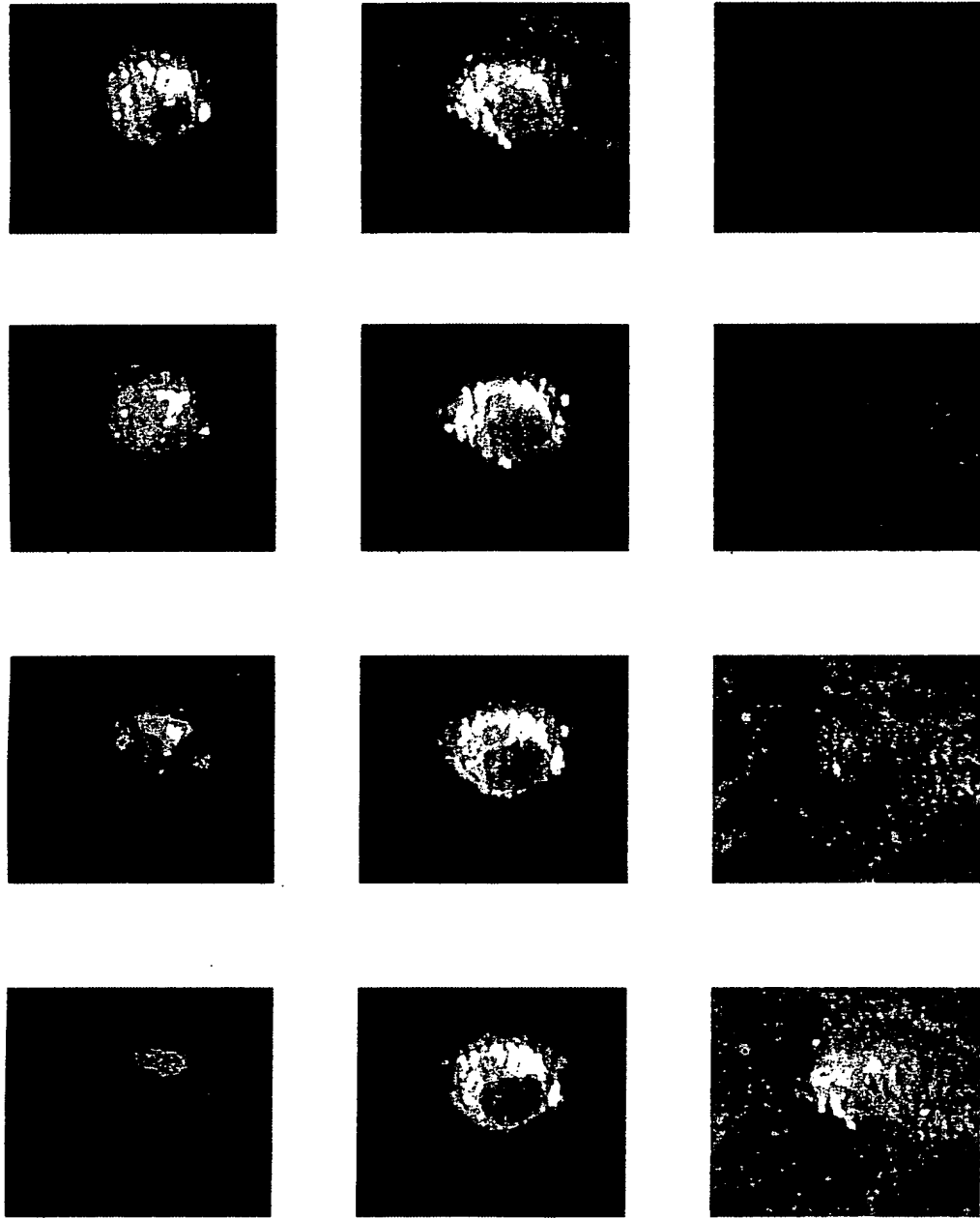




FIG. 17



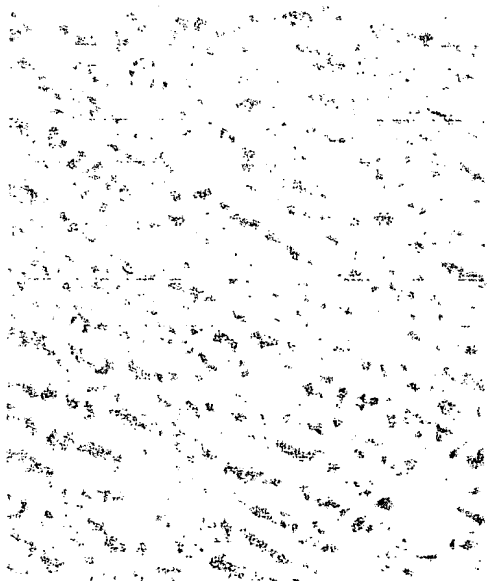
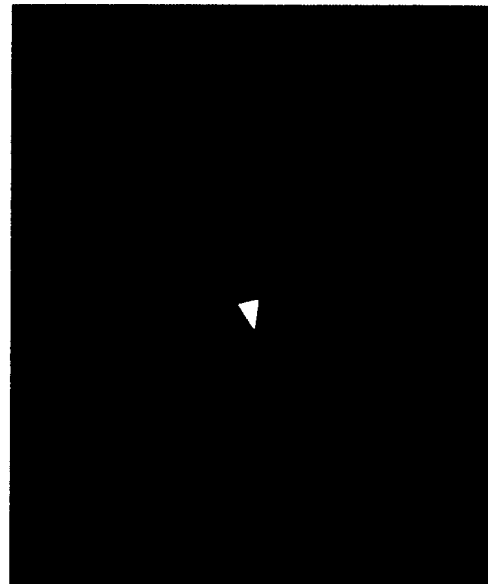
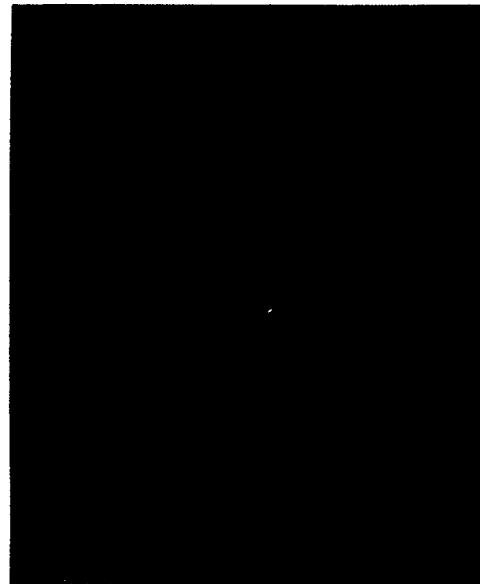
GREEN:ZO-1 / RED:MICROGLIA / BLUE:NUCLEUS

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FIG. 18

PHASE

PKH26 -STAINED Mi



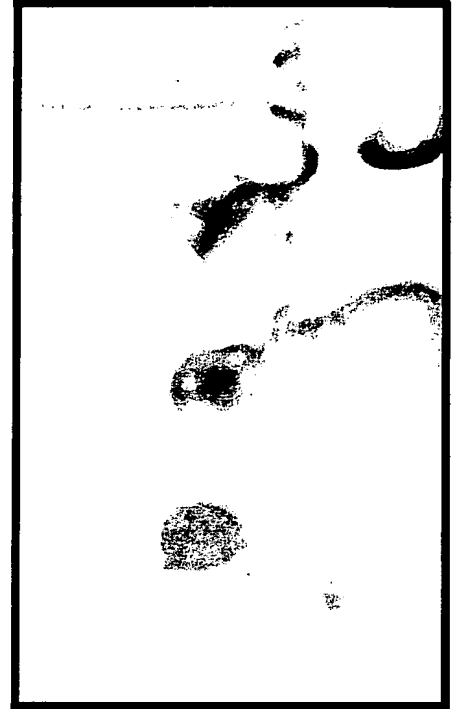
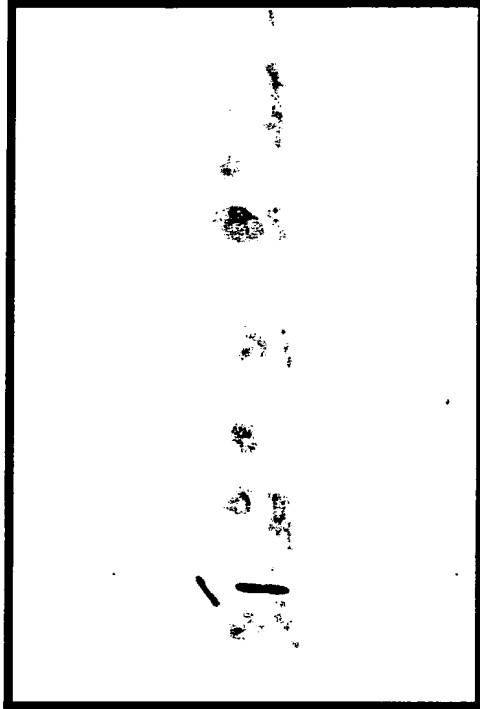
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ACTIVITY AND USES THEREOF (As Amended)

Inventor(s): Makoto SAWADA  
DOCKET NO.: 084335-0201

FIG. 19

MBEC4+Raw264.7



MBEC4+6-3



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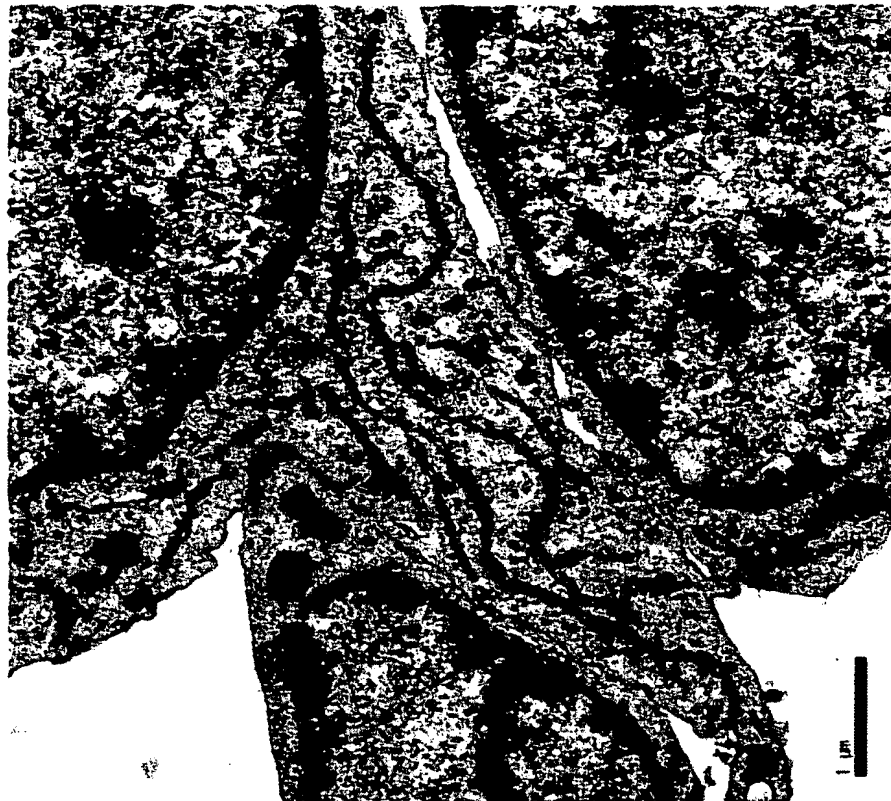
FIG. 20



0.2  $\mu$  m

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FIG. 21



1 μm

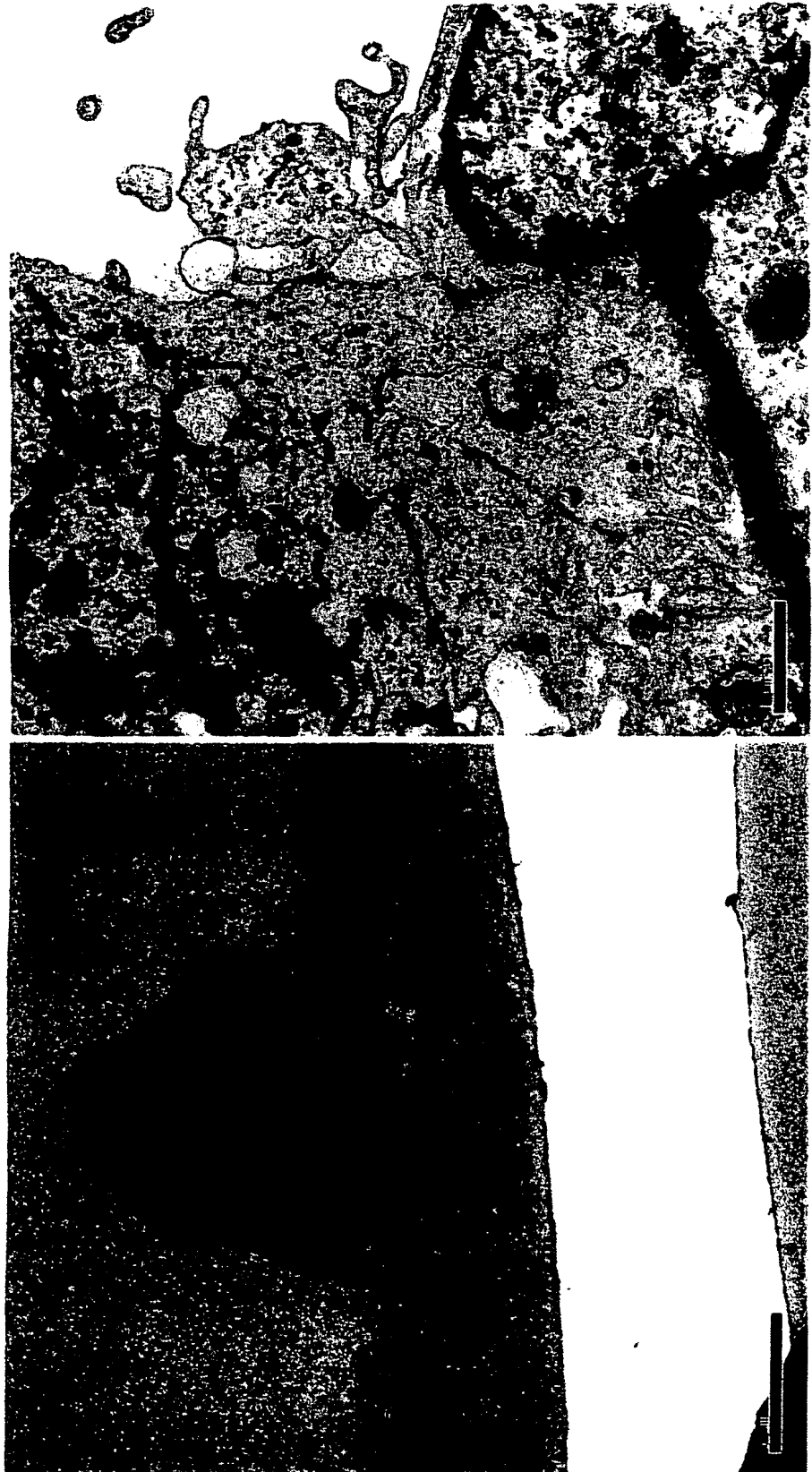


5 μm

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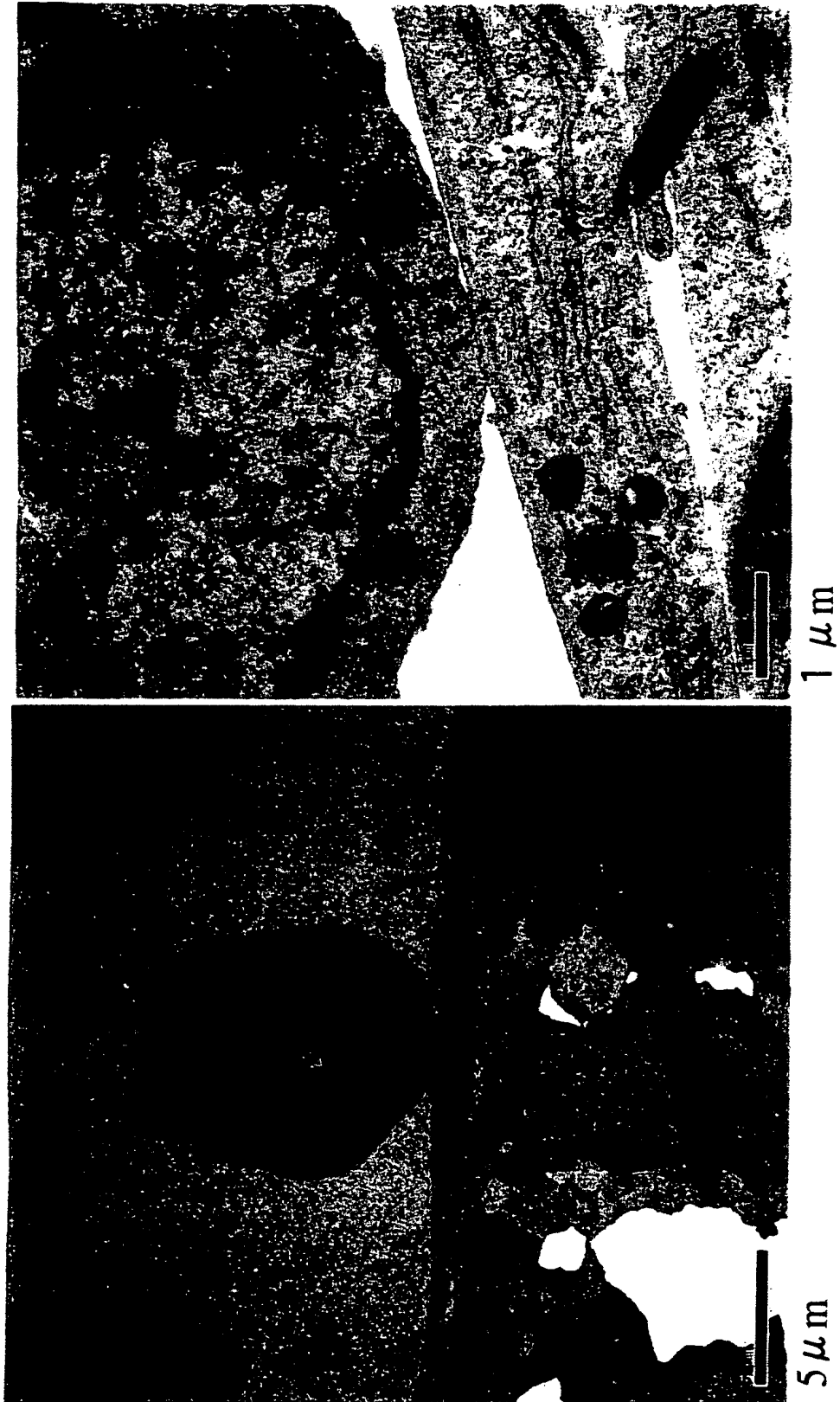
FIG. 22



1 μm

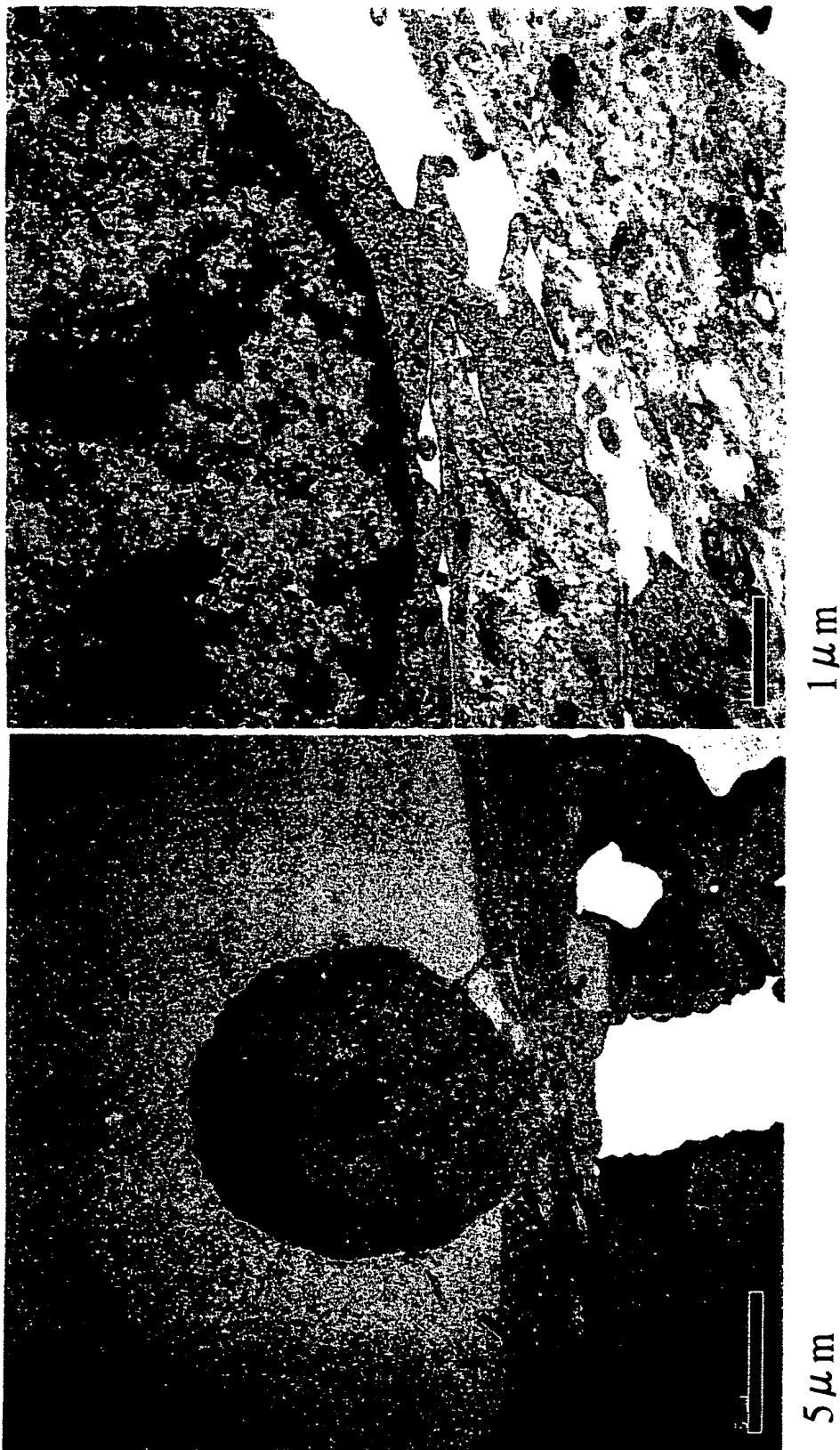
5 μm

FIG. 23



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FIG. 24





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